

ADY-001B

SEQUENCE LISTING

<110> Brooks, Cydney C.

<120> USE OF INSULIN RESPONSE MODULATORS IN THE
TREATMENT OF DIABETES AND INSULIN RESISTANCE

<130> ADY-001B

<150> 60/406,618

<151> 2002-08-27

<160> 3

<170> FastSEQ for Windows Version 4.0

 $\langle 210 \rangle$ 1

<211> 1025

<212> PRT

<213> Homo sapiens

<400> 1

| | | | | | | | | | | | | | | | |
|------------|------------|------------|------------|-----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Met 1 | Glu | Pro | Phe | Thr 5 | Asn | Asp | Arg | Leu | Gln 10 | Leu | Pro | Arg | Asn | Met 15 | Ile |
| Glu | Asn | Ser | Met 20 | Phe | Glu | Glu | Glu | Pro 25 | Asp | Val | Val | Asp | Leu 30 | Ala | Lys |
| Glu | Pro | Cys 35 | Leu | His | Pro | Leu | Glu 40 | Pro | Asp | Glu | Val | Glu 45 | Tyr | Glu | Pro |
| Arg | Gly 50 | Ser | Arg | Leu | Leu | Val 55 | Arg | Gly | Leu | Gly | Glu 60 | His | Glu | Met | Glu |
| Glu 65 | Asp | Glu | Glu | Asp 70 | Tyr | Glu | Ser | Ser | Ala | Lys 75 | Leu | Leu | Gly | Met 80 | Ser |
| Phe | Met | Asn | Arg | Ser 85 | Ser | Gly | Leu | Arg | Asn 90 | Ser | Ala | Thr | Gly | Tyr 95 | Arg |
| Gln | Ser | Pro | Asp 100 | Gly | Ala | Cys | Ser | Val 105 | Pro | Ser | Ala | Arg | Thr 110 | Met | Val |
| Val | Cys | Ala 115 | Phe | Val | Ile | Val | Val 120 | Ala | Val | Ser | Val | Ile 125 | Met | Val | Ile |
| Tyr 130 | Leu | Leu | Pro | Arg | Cys | Thr 135 | Phe | Thr | Lys | Glu | Gly 140 | Cys | His | Lys | Lys |
| Asn 145 | Gln | Ser | Ile | Gly | Leu 150 | Ile | Gln | Pro | Phe | Ala 155 | Thr | Asn | Gly | Lys | Leu 160 |
| Phe | Pro | Trp | Ala 165 | Gln | Ile | Arg | Leu | Pro | Thr 170 | Ala | Val | Val | Pro | Leu 175 | Arg |
| Tyr | Glu | Leu | Ser 180 | Leu | His | Pro | Asn 185 | Leu | Thr | Ser | Met | Thr | Phe 190 | Arg | Gly |
| Ser | Val | Thr 195 | Ile | Ser | Val | Gln | Ala 200 | Leu | Gln | Val | Thr | Trp 205 | Asn | Ile | Ile |
| Leu | His 210 | Ser | Thr | Gly | His | Asn 215 | Ile | Ser | Arg | Val | Thr 220 | Phe | Met | Ser | Ala |
| Val 225 | Ser | Ser | Gln | Glu | Lys 230 | Gln | Ala | Glu | Ile | Leu 235 | Glu | Tyr | Ala | Tyr | His 240 |
| Gly | Gln | Ile | Ala 245 | Ile | Val | Ala | Pro | Glu | Ala 250 | Leu | Leu | Ala | Gly | His 255 | Asn |
| Tyr | Thr | Leu | Lys 260 | Ile | Glu | Tyr | Ser | Ala 265 | Asn | Ile | Ser | Ser | Ser 270 | Tyr | Tyr |
| Gly | Phe | Tyr | Gly | Phe | Ser | Tyr | Thr | Asp | Glu | Ser | Asn | Glu | Lys | Lys | Tyr |

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| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Phe | Ala | Ala | Thr | Gln | Phe | Glu | Pro | Leu | Ala | Ala | Arg | Ser | Ala | Phe | Pro |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Cys | Phe | Asp | Glu | Pro | Ala | Phe | Lys | Ala | Thr | Phe | Ile | Ile | Lys | Ile | Ile |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Arg | Asp | Glu | Gln | Tyr | Thr | Ala | Leu | Ser | Asn | Met | Pro | Lys | Lys | Ser | Ser |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Val | Val | Leu | Asp | Asp | Gly | Leu | Val | Gln | Asp | Glu | Phe | Ser | Glu | Ser | Val |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Lys | Met | Ser | Thr | Tyr | Leu | Val | Ala | Phe | Ile | Val | Gly | Glu | Met | Lys | Asn |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Leu | Ser | Gln | Asp | Val | Asn | Gly | Thr | Leu | Val | Ser | Ile | Tyr | Ala | Val | Pro |
| | 370 | | | | | 375 | | | | | 380 | | | | |
| Glu | Lys | Ile | Gly | Gln | Val | His | Tyr | Ala | Leu | Glu | Thr | Thr | Val | Lys | Leu |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Leu | Glu | Phe | Phe | Gln | Asn | Tyr | Phe | Glu | Ile | Gln | Tyr | Pro | Leu | Lys | Lys |
| | | | | 405 | | | | 410 | | | | | 415 | | |
| Leu | Asp | Leu | Val | Ala | Ile | Pro | Asp | Phe | Glu | Ala | Gly | Ala | Met | Glu | Asn |
| | | 420 | | | | | | 425 | | | | 430 | | | |
| Trp | Gly | Leu | Leu | Thr | Phe | Arg | Glu | Glu | Thr | Leu | Leu | Tyr | Asp | Ser | Asn |
| | 435 | | | | | | 440 | | | | | 445 | | | |
| Thr | Ser | Ser | Met | Ala | Asp | Arg | Lys | Leu | Val | Thr | Lys | Ile | Ile | Ala | His |
| | 450 | | | | | 455 | | | | | 460 | | | | |
| Glu | Leu | Ala | His | Gln | Trp | Phe | Gly | Asn | Leu | Val | Thr | Met | Lys | Trp | Trp |
| 465 | | | | | 470 | | | | 475 | | | | | | 480 |
| Asn | Asp | Leu | Trp | Leu | Asn | Glu | Gly | Phe | Ala | Thr | Phe | Met | Glu | Tyr | Phe |
| | | | | 485 | | | | 490 | | | | | 495 | | |
| Ser | Leu | Glu | Lys | Ile | Phe | Lys | Glu | Leu | Ser | Ser | Tyr | Glu | Asp | Phe | Leu |
| | | 500 | | | | | 505 | | | | | 510 | | | |
| Asp | Ala | Arg | Phe | Lys | Thr | Met | Lys | Lys | Asp | Ser | Leu | Asn | Ser | Ser | His |
| | 515 | | | | | | 520 | | | | | 525 | | | |
| Pro | Ile | Ser | Ser | Ser | Val | Gln | Ser | Ser | Glu | Gln | Ile | Glu | Glu | Met | Phe |
| | 530 | | | | | 535 | | | | | 540 | | | | |
| Asp | Ser | Leu | Ser | Tyr | Phe | Lys | Gly | Ser | Ser | Leu | Leu | Leu | Met | Leu | Lys |
| 545 | | | | | 550 | | | | 555 | | | | | | 560 |
| Thr | Tyr | Leu | Ser | Glu | Asp | Val | Phe | Gln | His | Ala | Val | Val | Leu | Tyr | Leu |
| | | | | 565 | | | | 570 | | | | | 575 | | |
| His | Asn | His | Ser | Tyr | Ala | Ser | Ile | Gln | Ser | Asp | Asp | Leu | Trp | Asp | Ser |
| | | | 580 | | | | | 585 | | | | 590 | | | |
| Phe | Asn | Glu | Val | Thr | Asn | Gln | Thr | Leu | Asp | Val | Lys | Arg | Met | Met | Lys |
| | 595 | | | | | 600 | | | | | 605 | | | | |
| Thr | Trp | Thr | Leu | Gln | Lys | Gly | Phe | Pro | Leu | Val | Thr | Val | Gln | Lys | Lys |
| | 610 | | | | | 615 | | | | | 620 | | | | |
| Gly | Lys | Glu | Leu | Phe | Ile | Gln | Gln | Glu | Arg | Phe | Phe | Leu | Asn | Met | Lys |
| 625 | | | | | 630 | | | | 635 | | | | | | 640 |
| Pro | Glu | Ile | Gln | Pro | Ser | Asp | Thr | Ser | Tyr | Leu | Trp | His | Ile | Pro | Leu |
| | | | | 645 | | | | 650 | | | | | 655 | | |
| Ser | Tyr | Val | Thr | Glu | Gly | Arg | Asn | Tyr | Ser | Lys | Tyr | Gln | Ser | Val | Ser |
| | | 660 | | | | | 665 | | | | | 670 | | | |
| Leu | Leu | Asp | Lys | Lys | Ser | Gly | Val | Ile | Asn | Leu | Thr | Glu | Glu | Val | Leu |
| | | 675 | | | | | 680 | | | | | 685 | | | |
| Trp | Val | Lys | Val | Asn | Ile | Asn | Met | Asn | Gly | Tyr | Tyr | Ile | Val | His | Tyr |
| | 690 | | | | | 695 | | | | | 700 | | | | |
| Ala | Asp | Asp | Asp | Trp | Glu | Ala | Leu | Ile | His | Gln | Leu | Lys | Ile | Asn | Pro |
| 705 | | | | | 710 | | | | 715 | | | | | | 720 |
| Tyr | Val | Leu | Ser | Asp | Lys | Asp | Arg | Ala | Asn | Leu | Ile | Asn | Asn | Ile | Phe |
| | | | | 725 | | | | | 730 | | | | | 735 | |

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Glu Leu Ala Gly Leu Gly Lys Val Pro Leu Lys Arg Ala Phe Asp Leu
 740 745 750
 Ile Asn Tyr Leu Gly Asn Glu Asn His Thr Ala Pro Ile Thr Glu Ala
 755 760 765
 Leu Phe Gln Thr Asp Leu Ile Tyr Asn Leu Leu Glu Lys Leu Gly Tyr
 770 775 780
 Met Asp Leu Ala Ser Arg Leu Val Thr Arg Val Phe Lys Leu Leu Gln
 785 790 795 800
 Asn Gln Ile Gln Gln Gln Thr Trp Thr Asp Glu Gly Thr Pro Ser Met
 805 810 815
 Arg Glu Leu Arg Ser Ala Leu Leu Glu Phe Ala Cys Thr His Asn Leu
 820 825 830
 Gly Asn Cys Ser Thr Thr Ala Met Lys Leu Phe Asp Asp Trp Met Ala
 835 840 845
 Ser Asn Gly Thr Gln Ser Leu Pro Thr Asp Val Met Thr Val Phe
 850 855 860
 Lys Val Gly Ala Lys Thr Asp Lys Gly Trp Ser Phe Leu Leu Gly Lys
 865 870 875 880
 Tyr Ile Ser Ile Gly Ser Glu Ala Glu Lys Asn Lys Ile Leu Glu Ala
 885 890 895
 Leu Ala Ser Ser Glu Asp Val Arg Lys Leu Tyr Trp Leu Met Lys Ser
 900 905 910
 Ser Leu Asn Gly Asp Asn Phe Arg Thr Gln Lys Leu Ser Phe Ile Ile
 915 920 925
 Arg Thr Val Gly Arg His Phe Pro Gly His Leu Leu Ala Trp Asp Phe
 930 935 940
 Val Lys Glu Asn Trp Asn Lys Leu Val Gln Lys Phe Pro Leu Gly Ser
 945 950 955 960
 Tyr Thr Ile Gln Asn Ile Val Ala Gly Ser Thr Tyr Leu Phe Ser Thr
 965 970 975
 Lys Thr His Leu Ser Glu Val Gln Ala Phe Phe Glu Asn Gln Ser Glu
 980 985 990
 Ala Thr Phe Arg Leu Arg Cys Val Gln Glu Ala Leu Glu Val Ile Gln
 995 1000 1005
 Leu Asn Ile Gln Trp Met Glu Lys Asn Leu Lys Ser Leu Thr Trp Trp
 1010 1015 1020
 Leu
 1025

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<211> 1025

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<400> 2

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 20 25 30
 Glu Pro Cys Leu His Pro Leu Glu Pro Asp Glu Val Glu Tyr Glu Pro
 35 40 45
 Arg Gly Ser Arg Leu Leu Val Arg Gly Leu Gly Glu His Glu Met Asp
 50 55 60
 Glu Asp Glu Glu Asp Tyr Glu Ser Ser Ala Lys Leu Leu Gly Met Ser
 65 70 75 80
 Phe Met Asn Arg Ser Ser Gly Leu Arg Asn Ser Ala Thr Gly Tyr Arg

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| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| | | | | 85 | | | | | 90 | | | | | 95 | | | |
| Gln | Ser | Pro | Asp | Gly | Thr | Cys | Ser | Val | Pro | Ser | Ala | Arg | Thr | Leu | Val | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | |
| Ile | Cys | Val | Phe | Val | Ile | Val | Val | Ala | Val | Ser | Val | Ile | Met | Val | Ile | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | |
| Tyr | Leu | Leu | Pro | Arg | Cys | Thr | Phe | Thr | Lys | Glu | Gly | Cys | His | Lys | Thr | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | | |
| Asn | Gln | Ser | Ala | Glu | Leu | Ile | Gln | Pro | Ile | Ala | Thr | Asn | Gly | Lys | Val | | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | | |
| Phe | Pro | Trp | Ala | Gln | Ile | Arg | Leu | Pro | Thr | Ala | Ile | Ile | Pro | Gln | Arg | | |
| | | | 165 | | | | | | 170 | | | | | 175 | | | |
| Tyr | Glu | Leu | Ser | Leu | His | Pro | Asn | Leu | Thr | Ser | Met | Thr | Phe | Arg | Gly | | |
| | | 180 | | | | | 185 | | | | | | 190 | | | | |
| Ser | Val | Thr | Ile | Ser | Leu | Gln | Ala | Leu | Gln | Asp | Thr | Arg | Asp | Ile | Ile | | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | |
| Leu | His | Ser | Thr | Gly | His | Asn | Ile | Ser | Ser | Val | Thr | Phe | Met | Ser | Ala | | |
| | 210 | | | | | 215 | | | | | 220 | | | | | | |
| Val | Ser | Ser | Gln | Glu | Lys | Gln | Val | Glu | Ile | Leu | Glu | Tyr | Pro | Tyr | His | | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | | |
| Glu | Gln | Ile | Ala | Val | Val | Ala | Pro | Glu | Ser | Leu | Leu | Thr | Gly | His | Asn | | |
| | | | 245 | | | | | | 250 | | | | | 255 | | | |
| Tyr | Thr | Leu | Lys | Ile | Glu | Tyr | Ser | Ala | Asn | Ile | Ser | Asn | Ser | Tyr | Tyr | | |
| | | 260 | | | | | 265 | | | | | | | 270 | | | |
| Gly | Phe | Tyr | Gly | Ile | Thr | Tyr | Thr | Asp | Lys | Ser | Asn | Glu | Lys | Lys | Asn | | |
| | 275 | | | | | | 280 | | | | | 285 | | | | | |
| Phe | Ala | Ala | Thr | Gln | Phe | Glu | Pro | Leu | Ala | Ala | Arg | Ser | Ala | Phe | Pro | | |
| | 290 | | | | | 295 | | | | | 300 | | | | | | |
| Cys | Phe | Asp | Glu | Pro | Ala | Phe | Lys | Ala | Thr | Phe | Ile | Ile | Lys | Ile | Thr | | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | | |
| Arg | Asp | Glu | His | His | Thr | Ala | Leu | Ser | Asn | Met | Pro | Lys | Lys | Ser | Ser | | |
| | | | 325 | | | | | | 330 | | | | | 335 | | | |
| Val | Pro | Thr | Glu | Glu | Gly | Leu | Ile | Gln | Asp | Glu | Phe | Ser | Glu | Ser | Val | | |
| | | 340 | | | | | | 345 | | | | | 350 | | | | |
| Lys | Met | Ser | Thr | Tyr | Leu | Val | Ala | Phe | Ile | Val | Gly | Glu | Met | Arg | Asn | | |
| | 355 | | | | | 360 | | | | | | 365 | | | | | |
| Leu | Ser | Gln | Asp | Val | Asn | Gly | Thr | Leu | Val | Ser | Val | Tyr | Ala | Val | Pro | | |
| | 370 | | | | | 375 | | | | | 380 | | | | | | |
| Glu | Lys | Ile | Asp | Gln | Val | Tyr | His | Ala | Leu | Asp | Thr | Thr | Val | Lys | Leu | | |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 | | |
| Leu | Glu | Phe | Tyr | Gln | Asn | Tyr | Phe | Glu | Ile | Gln | Tyr | Pro | Leu | Lys | Lys | | |
| | | | 405 | | | | | 410 | | | | | | 415 | | | |
| Leu | Asp | Leu | Val | Ala | Ile | Pro | Asp | Phe | Glu | Ala | Gly | Ala | Met | Glu | Asn | | |
| | | 420 | | | | | | 425 | | | | | 430 | | | | |
| Trp | Gly | Leu | Leu | Thr | Phe | Arg | Glu | Glu | Thr | Leu | Leu | Tyr | Asp | Asn | Ala | | |
| | 435 | | | | | 440 | | | | | | 445 | | | | | |
| Thr | Ser | Ser | Val | Ala | Asp | Arg | Lys | Leu | Val | Thr | Lys | Ile | Ile | Ala | His | | |
| | 450 | | | | | 455 | | | | | 460 | | | | | | |
| Glu | Leu | Ala | His | Gln | Trp | Phe | Gly | Asn | Leu | Val | Thr | Met | Gln | Trp | Trp | | |
| 465 | | | | | 470 | | | | | 475 | | | | | 480 | | |
| Asn | Asp | Leu | Trp | Leu | Asn | Glu | Gly | Phe | Ala | Thr | Phe | Met | Glu | Tyr | Phe | | |
| | | | 485 | | | | | 490 | | | | | | 495 | | | |
| Ser | Val | Glu | Lys | Ile | Phe | Lys | Glu | Leu | Asn | Ser | Tyr | Glu | Asp | Phe | Leu | | |
| | | 500 | | | | | | 505 | | | | | 510 | | | | |
| Asp | Ala | Arg | Phe | Lys | Thr | Met | Arg | Lys | Asp | Ser | Leu | Asn | Ser | Ser | His | | |
| | 515 | | | | | | 520 | | | | | 525 | | | | | |
| Pro | Ile | Ser | Ser | Ser | Val | Gln | Ser | Ser | Glu | Gln | Ile | Glu | Glu | Met | Phe | | |
| | 530 | | | | | 535 | | | | | 540 | | | | | | |

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| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Ser | Leu | Ser | Tyr | Phe | Lys | Gly | Ala | Ser | Leu | Leu | Leu | Met | Leu | Lys |
| 545 | | | | | 550 | | | | | 555 | | | | | 560 |
| Ser | Tyr | Leu | Ser | Glu | Asp | Val | Phe | Gln | His | Ala | Ile | Ile | Leu | Tyr | Leu |
| | | | | 565 | | | | | 570 | | | | | 575 | |
| His | Asn | His | Ser | Tyr | Ala | Ala | Ile | Gln | Ser | Asp | Asp | Leu | Trp | Asp | Ser |
| | | | 580 | | | | | 585 | | | | | 590 | | |
| Phe | Asn | Glu | Val | Thr | Gly | Lys | Thr | Leu | Asp | Val | Lys | Lys | Met | Met | Lys |
| | | 595 | | | | | 600 | | | | | 605 | | | |
| Thr | Trp | Thr | Leu | Gln | Lys | Gly | Phe | Pro | Leu | Val | Thr | Val | Gln | Arg | Lys |
| | 610 | | | | | 615 | | | | | 620 | | | | |
| Gly | Thr | Glu | Leu | Leu | Leu | Gln | Gln | Glu | Arg | Phe | Phe | Pro | Ser | Met | Gln |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| Pro | Glu | Ile | Gln | Asp | Ser | Asp | Thr | Ser | His | Leu | Trp | His | Ile | Pro | Ile |
| | | | | 645 | | | | | 650 | | | | | 655 | |
| Ser | Tyr | Val | Thr | Asp | Gly | Arg | Asn | Tyr | Ser | Glu | Tyr | Arg | Ser | Val | Ser |
| | | | 660 | | | | | 665 | | | | | 670 | | |
| Leu | Leu | Asp | Lys | Lys | Ser | Asp | Val | Ile | Asn | Leu | Thr | Glu | Gln | Val | Gln |
| | | 675 | | | | | 680 | | | | | 685 | | | |
| Trp | Val | Lys | Val | Asn | Thr | Asn | Met | Thr | Gly | Tyr | Tyr | Ile | Val | His | Tyr |
| | 690 | | | | | 695 | | | | | 700 | | | | |
| Ala | His | Asp | Gly | Trp | Ala | Ala | Leu | Ile | Asn | Gln | Leu | Lys | Arg | Asn | Pro |
| 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| Tyr | Val | Leu | Ser | Asp | Lys | Asp | Arg | Ala | Asn | Leu | Ile | Asn | Asn | Ile | Phe |
| | | | | 725 | | | | | 730 | | | | | 735 | |
| Glu | Leu | Ala | Gly | Leu | Gly | Lys | Val | Pro | Leu | Gln | Met | Ala | Phe | Asp | Leu |
| | | | 740 | | | | | 745 | | | | | 750 | | |
| Ile | Asp | Tyr | Leu | Arg | Asn | Glu | Thr | His | Thr | Ala | Pro | Ile | Thr | Glu | Ala |
| | | 755 | | | | | 760 | | | | | 765 | | | |
| Leu | Phe | Gln | Thr | Asp | Leu | Ile | Tyr | Asn | Leu | Leu | Glu | Lys | Leu | Gly | His |
| | 770 | | | | | 775 | | | | | 780 | | | | |
| Met | Asp | Leu | Ser | Ser | Arg | Leu | Val | Thr | Arg | Val | His | Lys | Leu | Leu | Gln |
| 785 | | | | | 790 | | | | | 795 | | | | | 800 |
| Asn | Gln | Ile | Gln | Gln | Gln | Thr | Trp | Thr | Asp | Glu | Gly | Thr | Pro | Ser | Met |
| | | | | 805 | | | | | 810 | | | | | 815 | |
| Arg | Glu | Leu | Arg | Ser | Ala | Leu | Leu | Glu | Phe | Ala | Cys | Ala | His | Ser | Leu |
| | | | 820 | | | | | 825 | | | | | 830 | | |
| Glu | Asn | Cys | Thr | Thr | Met | Ala | Thr | Lys | Leu | Phe | Asp | Gly | Trp | Met | Ala |
| | | 835 | | | | | 840 | | | | | 845 | | | |
| Ser | Asn | Gly | Thr | Gln | Ser | Leu | Pro | Thr | Asp | Val | Met | Thr | Thr | Val | Phe |
| | 850 | | | | | 855 | | | | | 860 | | | | |
| Lys | Val | Gly | Ala | Arg | Thr | Glu | Lys | Gly | Trp | Leu | Phe | Leu | Phe | Ser | Met |
| 865 | | | | | 870 | | | | | 875 | | | | | 880 |
| Tyr | Ser | Ser | Met | Gly | Ser | Glu | Ala | Glu | Lys | Asp | Lys | Ile | Leu | Glu | Ala |
| | | | | 885 | | | | | 890 | | | | | 895 | |
| Leu | Ala | Ser | Ser | Ala | Asp | Ala | His | Lys | Leu | Tyr | Trp | Leu | Met | Lys | Ser |
| | | | 900 | | | | | 905 | | | | | 910 | | |
| Ser | Leu | Asp | Gly | Asp | Ile | Ile | Arg | Thr | Gln | Lys | Leu | Ser | Leu | Ile | Ile |
| | | 915 | | | | | 920 | | | | | 925 | | | |
| Arg | Thr | Val | Gly | Arg | Gln | Phe | Pro | Gly | His | Leu | Leu | Ala | Trp | Asp | Phe |
| | 930 | | | | | 935 | | | | | | 940 | | | |
| Val | Lys | Glu | Asn | Trp | Asn | Lys | Leu | Val | His | Lys | Phe | His | Leu | Gly | Ser |
| 945 | | | | | 950 | | | | | 955 | | | | | 960 |
| Tyr | Thr | Ile | Gln | Ser | Ile | Val | Ala | Gly | Ser | Thr | His | Leu | Phe | Ser | Thr |
| | | | | 965 | | | | | 970 | | | | | 975 | |
| Lys | Thr | His | Leu | Ser | Glu | Val | Gln | Glu | Phe | Phe | Glu | Asn | Gln | Ser | Glu |
| | | | 980 | | | | | 985 | | | | | 990 | | |
| Ala | Thr | Leu | Gln | Leu | Arg | Cys | Val | Gln | Glu | Ala | Phe | Glu | Val | Ile | Glu |

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```

          995              1000              1005
Leu Asn Ile Gln Trp Met Ala Arg Asn Leu Lys Thr Leu Thr Leu Trp
    1010              1015              1020
Leu
1025

```

```

<210> 3
<211> 962
<212> PRT
<213> Homo sapiens

```

```

<400> 3
Met Asn Phe Leu Arg Gly Val Met Gly Gly Gln Ser Ala Gly Pro Gln
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His Thr Glu Ala Glu Thr Ile Gln Lys Leu Cys Asp Arg Val Ala Ser
    20          25          30
Ser Thr Leu Leu Asp Asp Arg Arg Asn Ala Val Arg Ala Leu Lys Ser
    35          40          45
Leu Ser Lys Lys Tyr Arg Leu Glu Val Gly Ile Gln Ala Met Glu His
    50          55          60
Leu Ile His Val Leu Gln Thr Asp Arg Ser Asp Ser Glu Ile Ile Gly
    65          70          75          80
Tyr Ala Leu Asp Ile Leu Tyr Asn Ile Ile Ser Asn Glu Glu Glu Glu
    85          90          95
Glu Val Glu Glu Asn Ser Thr Arg Gln Ser Glu Asp Leu Gly Ser Gln
    100          105          110
Phe Thr Glu Ile Phe Ile Lys Gln Gln Glu Asn Val Thr Leu Leu Leu
    115          120          125
Ser Leu Leu Glu Glu Phe Asp Phe His Val Arg Trp Pro Gly Val Lys
    130          135          140
Leu Leu Thr Ser Leu Leu Lys Gln Leu Gly Pro Gln Val Gln Gln Ile
    145          150          155          160
Ile Leu Val Ser Pro Met Gly Val Ser Arg Leu Met Asp Leu Leu Ala
    165          170          175
Asp Ser Arg Glu Val Ile Arg Asn Asp Gly Val Leu Leu Leu Gln Ala
    180          185          190
Leu Thr Arg Ser Asn Gly Ala Ile Gln Lys Ile Val Ala Phe Glu Asn
    195          200          205
Ala Phe Glu Arg Leu Leu Asp Ile Ile Ser Glu Glu Gly Asn Ser Asp
    210          215          220
Gly Gly Ile Val Val Glu Asp Cys Leu Ile Leu Leu Gln Asn Leu Leu
    225          230          235          240
Lys Asn Asn Asn Ser Asn Gln Asn Phe Phe Lys Glu Gly Ser Tyr Ile
    245          250          255
Gln Arg Met Lys Pro Trp Phe Glu Val Gly Asp Glu Asn Ser Gly Trp
    260          265          270
Ser Ala Gln Lys Val Thr Asn Leu His Leu Met Leu Gln Leu Val Arg
    275          280          285
Val Leu Val Ser Pro Thr Asn Pro Pro Gly Ala Thr Ser Ser Cys Gln
    290          295          300
Lys Ala Met Phe Gln Cys Gly Leu Leu Gln Gln Leu Cys Thr Ile Leu
    305          310          315          320
Met Ala Thr Gly Val Pro Ala Asp Ile Leu Thr Glu Thr Ile Asn Thr
    325          330          335
Val Ser Glu Val Ile Arg Gly Cys Gln Val Asn Gln Asp Tyr Phe Ala
    340          345          350

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ADY-001B

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Val | Asn | Ala | Pro | Ser | Asn | Pro | Pro | Arg | Pro | Ala | Ile | Val | Val | Leu |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Leu | Met | Ser | Met | Val | Asn | Glu | Arg | Gln | Pro | Phe | Val | Leu | Arg | Cys | Ala |
| | 370 | | | | | 375 | | | | | 380 | | | | |
| Val | Leu | Tyr | Cys | Phe | Gln | Cys | Phe | Leu | Tyr | Lys | Asn | Gln | Lys | Gly | Gln |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Gly | Glu | Ile | Val | Ser | Thr | Leu | Leu | Pro | Ser | Thr | Ile | Asp | Ala | Thr | Gly |
| | | | | 405 | | | | | 410 | | | | | 415 | |
| Asn | Ser | Val | Ser | Ala | Gly | Gln | Leu | Leu | Cys | Gly | Gly | Leu | Phe | Ser | Thr |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Asp | Ser | Leu | Ser | Asn | Trp | Cys | Ala | Ala | Val | Ala | Leu | Ala | His | Ala | Leu |
| | 435 | | | | | | 440 | | | | | 445 | | | |
| Gln | Glu | Asn | Ala | Thr | Gln | Lys | Glu | Gln | Leu | Leu | Arg | Val | Gln | Leu | Ala |
| | 450 | | | | | 455 | | | | | 460 | | | | |
| Thr | Ser | Ile | Gly | Asn | Pro | Pro | Val | Ser | Leu | Leu | Gln | Gln | Cys | Thr | Asn |
| 465 | | | | | 470 | | | | | 475 | | | | | 480 |
| Ile | Leu | Ser | Gln | Gly | Ser | Lys | Ile | Gln | Thr | Arg | Val | Gly | Leu | Leu | Met |
| | | | 485 | | | | | | 490 | | | | | 495 | |
| Leu | Leu | Cys | Thr | Trp | Leu | Ser | Asn | Cys | Pro | Ile | Ala | Val | Thr | His | Phe |
| | | | 500 | | | | | 505 | | | | | 510 | | |
| Leu | His | Asn | Ser | Ala | Asn | Val | Pro | Phe | Leu | Thr | Gly | Gln | Ile | Ala | Glu |
| | | 515 | | | | | 520 | | | | | 525 | | | |
| Asn | Leu | Gly | Glu | Glu | Glu | Gln | Leu | Val | Gln | Gly | Leu | Cys | Ala | Leu | Leu |
| | 530 | | | | | 535 | | | | | 540 | | | | |
| Leu | Gly | Ile | Ser | Ile | Tyr | Phe | Asn | Asp | Asn | Ser | Leu | Glu | Ser | Tyr | Met |
| 545 | | | | | 550 | | | | | 555 | | | | | 560 |
| Lys | Glu | Lys | Leu | Lys | Gln | Leu | Ile | Glu | Lys | Arg | Ile | Gly | Lys | Glu | Asn |
| | | | | 565 | | | | | 570 | | | | | 575 | |
| Phe | Ile | Glu | Lys | Leu | Gly | Phe | Ile | Ser | Lys | His | Glu | Leu | Tyr | Ser | Arg |
| | | | 580 | | | | | 585 | | | | | 590 | | |
| Ala | Ser | Gln | Lys | Pro | Gln | Pro | Asn | Phe | Pro | Ser | Pro | Glu | Tyr | Met | Ile |
| | | 595 | | | | | 600 | | | | | 605 | | | |
| Phe | Asp | His | Glu | Phe | Thr | Lys | Leu | Val | Lys | Glu | Leu | Glu | Gly | Val | Ile |
| | 610 | | | | | 615 | | | | | 620 | | | | |
| Thr | Lys | Ala | Ile | Tyr | Lys | Ser | Ser | Glu | Glu | Asp | Lys | Lys | Glu | Glu | Glu |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| Val | Lys | Lys | Thr | Leu | Glu | Gln | His | Asp | Asn | Ile | Val | Thr | His | Tyr | Lys |
| | | | 645 | | | | | 650 | | | | | | 655 | |
| Asn | Met | Ile | Arg | Glu | Gln | Asp | Leu | Gln | Leu | Glu | Glu | Leu | Arg | Gln | Gln |
| | | 660 | | | | | 665 | | | | | | 670 | | |
| Val | Ser | Thr | Leu | Lys | Cys | Gln | Asn | Glu | Gln | Leu | Gln | Thr | Ala | Val | Thr |
| | | 675 | | | | | 680 | | | | | 685 | | | |
| Gln | Gln | Val | Ser | Gln | Ile | Gln | Gln | His | Lys | Asp | Gln | Tyr | Asn | Leu | Leu |
| | 690 | | | | | 695 | | | | | 700 | | | | |
| Lys | Ile | Gln | Leu | Gly | Lys | Asp | Asn | Gln | His | Gln | Gly | Ser | Tyr | Ser | Glu |
| 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| Gly | Ala | Gln | Met | Asn | Gly | Ile | Gln | Pro | Glu | Glu | Ile | Gly | Arg | Leu | Arg |
| | | | 725 | | | | | 730 | | | | | 735 | | |
| Glu | Glu | Ile | Glu | Glu | Leu | Lys | Arg | Asn | Gln | Glu | Leu | Leu | Gln | Ser | Gln |
| | | | 740 | | | | 745 | | | | | | 750 | | |
| Leu | Thr | Glu | Lys | Asp | Ser | Met | Ile | Glu | Asn | Met | Lys | Ser | Ser | Gln | Thr |
| | 755 | | | | | 760 | | | | | | 765 | | | |
| Ser | Gly | Thr | Asn | Glu | Gln | Ser | Ser | Ala | Ile | Val | Ser | Ala | Arg | Asp | Ser |
| | 770 | | | | | 775 | | | | | 780 | | | | |
| Glu | Gln | Val | Ala | Glu | Leu | Lys | Gln | Glu | Leu | Ala | Thr | Leu | Lys | Ser | Gln |
| 785 | | | | | 790 | | | | | 795 | | | | | 800 |
| Leu | Asn | Ser | Gln | Ser | Val | Glu | Ile | Thr | Lys | Leu | Gln | Thr | Glu | Lys | Gln |

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| | | | | 805 | | | | | 810 | | | | | 815 | | | |
| Glu | Leu | Leu | Gln | Lys | Thr | Glu | Ala | Phe | Ala | Lys | Ser | Val | Glu | Val | Gln | | |
| | | | 820 | | | | | | 825 | | | | | 830 | | | |
| Gly | Glu | Thr | Glu | Thr | Ile | Ile | Ala | Thr | Lys | Thr | Thr | Asp | Val | Glu | Gly | | |
| | | 835 | | | | | 840 | | | | | 845 | | | | | |
| Arg | Leu | Ser | Ala | Leu | Leu | Gln | Glu | Thr | Lys | Glu | Leu | Lys | Asn | Glu | Ile | | |
| | 850 | | | | | 855 | | | | | 860 | | | | | | |
| Lys | Ala | Leu | Ser | Glu | Glu | Arg | Thr | Ala | Ile | Lys | Glu | Gln | Leu | Asp | Ser | | |
| 865 | | | | | 870 | | | | | 875 | | | | | 880 | | |
| Ser | Asn | Ser | Thr | Ile | Ala | Ile | Leu | Gln | Thr | Glu | Lys | Asp | Lys | Leu | Glu | | |
| | | | 885 | | | | | | 890 | | | | | 895 | | | |
| Leu | Glu | Ile | Thr | Asp | Ser | Lys | Lys | Glu | Gln | Asp | Asp | Leu | Leu | Val | Leu | | |
| | | | 900 | | | | | 905 | | | | | | 910 | | | |
| Leu | Ala | Asp | Gln | Asp | Gln | Lys | Ile | Leu | Ser | Leu | Lys | Asn | Lys | Leu | Lys | | |
| | | 915 | | | | | 920 | | | | | 925 | | | | | |
| Asp | Leu | Gly | His | Pro | Val | Glu | Glu | Glu | Asp | Glu | Leu | Glu | Ser | Gly | Asp | | |
| | 930 | | | | | 935 | | | | | 940 | | | | | | |
| Gln | Glu | Asp | Glu | Asp | Asp | Glu | Ser | Glu | Asp | Pro | Gly | Lys | Asp | Leu | Asp | | |
| 945 | | | | | 950 | | | | | 955 | | | | | 960 | | |
| His | Ile | | | | | | | | | | | | | | | | |